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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/716,619	11/20/2003	John P. Daley	IVGN 140.1 CON	6354

65482 7590 03/18/2008

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EXAMINER	
KIM, TAEYOON	

ART UNIT	PAPER NUMBER
1651	

MAIL DATE	DELIVERY MODE
03/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/716,619	DALEY ET AL.	
	Examiner	Art Unit	
	TAEYOON KIM	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *55,76,78-87 and 89-98* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *55,76,78-87 and 89-98* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Applicant's amendment and response filed on 12/27/2007 has been received and entered into the case.

Claims 1-54, 56-75, 77 and 88 have been canceled, and claims 55, 76, 78-87 and 89-98 are pending and have been considered on the merits. All arguments have been fully considered.

In the response to the previous office action, applicant asserted that there is no motivation to combine N-acetyl-cystein of Darfler in the serum-free medium of Smith et al., which contains albumin because of the assumption made in Darfler that the use of antioxidant compounds such as N-acetyl-cysteine for culturing lymphoid cells in serum free media lacking albumin, and the stability of N-acetyl-cysteine being improved in the absence of albumin. The examiner disagrees with this assertion as follows.

First of all, the teaching of Darfler combined with the serum-free medium comprising serum albumin of Smith et al. is not the specific medium of Darfler (serum-free, albumin-free medium), which lacks albumin, but N-acetyl-cysteine. N-acetyl-cysteine is well known in the art as an antioxidant, as disclosed in Darfler. The Darfler's medium lacking albumin is not considered to be the teaching to combine with the medium of Smith et al.

It appears that Darfler discloses that albumin might be the reason for the reduction of the stability of N-acetyl-cysteine. As discussed by Darfler, and also the reference that Darfler relied on for such assumption (Ormstad et al. 1984), when human

plasma (that is human serum, not albumin alone) caused reduction on N-acetyl-cysteine's stability. Although Darfler discloses about 50% of the plasma being albumin, there is no conclusive data to support that albumin is the cause of the reduction in N-acetyl-cysteine's stability. Even if Darfler's assumption that albumin is causing the reduction of the stability is considered to be correct, it is the function of N-acetyl-cysteine as an antioxidant rather than its stability. Since N-acetyl-cysteine is well known in the art as an antioxidant and can be used in the medium of Smith et al., a person of ordinary skill in the art would try to use N-acetyl-cysteine in the medium of Smith et al., unless the presence of albumin or other ingredient of the Smith et al.'s medium is completely abolish the activity of N-acetyl-cysteine.

A prior art reference that "teaches away" from the claimed invention is a significant factor to be considered in determining obviousness; however, "the nature of the teaching is highly relevant and must be weighed in substance. A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." In re Gurley, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994) (Claims were directed to an epoxy resin based printed circuit material. A prior art reference disclosed a polyester-imide resin based printed circuit material, and taught that although epoxy resin based materials have acceptable stability and some degree of flexibility, they are inferior to polyester-imide resin based materials. The court held the claims would have been obvious over the prior art because the reference taught epoxy resin based material was useful for

applicant's purpose, applicant did not distinguish the claimed epoxy from the prior art epoxy, and applicant asserted no discovery beyond what was known to the art.).

A person of ordinary skill in the art would recognize that there is finite number of antioxidants used in culture media, and N-acetyl-cysteine is one of such antioxidants, therefore, a person of ordinary skill in the art would try N-acetyl-cysteine as an antioxidant for culture medium of Smith et al. The Supreme Court recently states in KSR v. Teleflex (550 US82 USPQ2d 1385, 2007) "The same constricted analysis led the Court of Appeals to conclude, in error, that a patent claim cannot be proved obvious merely by showing that the combination of elements was "obvious to try." Id., at 289 (internal quotation marks omitted). When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under §103."

Furthermore, applicant argued that the lymphoid cells Darfler disccuses are hybiodoma cells, not CD34+ positive hematopoietic cells. This is not persuasive because the teaching of Darfler combined with Smith et al. is N-acetyl-cysteine not the cells or medium used in Darfler.

Still further, applicant argued that CD34 antigen on the surface of a cell serves as a marker of hematopoietic stem cells, and a person of ordinary skill in the art would not expect the growth requirements of mature lymphocytes to necessarily be the same as

those for a hemtopoietic stem cells. Applicant is reminded that there is no disclosure of the CD34+ hematopoietic cells being hematopoietic stem cells. It is claimed any hematopoietic cells having CD34 antigen expressed. Nevertheless, Smith et al. teach that the medium is for hematopoietic progenitor cells (see abstract), which include hematopoietic stem cells. The disclosure of lymphoids in Darfler is not the teaching combined with the medium and cells disclosed in Smith et al.

With regard to the two references (Walsh et al. and Hamilton et al.), these two references were introduced to provide supporting evidence that the recombinant CD34+ hematopoietic cells, rather than the teachings of the references are combined with the teaching of Smith et al. in view of Darfler. It is reminded that the rejection was written as "in light of Walsh et al. or Hamilton et al." not "in view of" or "in further view of" in the previous office action. Therefore, a rationale to combine these references with Smith et al. in view of Darfler is not required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 55, 76, 78-87 and 89-98 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. (WO 95/06112) in view of Darfler (US 4,927,762) in light of Walsh et al. (1994) and Hamilton et al. (WO 93/20195).

Claims are drawn to a serum-free eukaryotic cell culture medium comprising N-acetyl-L-cysteine and serum albumin, and a method of expanding recombinant CD34+ hematopoietic cells using a serum-free medium in suspension culture comprising N-acetyl-L-cysteine and serum albumin in the absence of stromal cells, and limitations to supplements including amino acids, cytokines, growth factors, glucocorticoid (hydrocortisone); limitations to the cells being expanded at 37°C for 6-8 days.

Smith et al. teach a method of expanding human CD34+ hematopoietic cells in suspension culture using a serum-free medium comprising human albumin (see Abstract), amino acids (see p.7, lines 5-12), cytokines (see Table 7), growth factors (see p.7, lines 14-24), and hydrocortisone (see p.9, lines 19-24). Smith et al. also teach the culture/expansion being at 37°C (see p.20 line 23) and for 5 to 7 days (see p.20, line 25). Smith et al. further teach administration of hematopoietic cells expanded to a patient (see p.14, lines 26-33).

Smith et al. do not teach the use of N-acetyl-L-cysteine in the culture medium.

Darfler teaches the use of antioxidant such as N-acetyl-L-cysteine (N-acetylcysteine) in the culture of lymphoid (see Abstract and Example 3).

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to use N-acetyl-L-cysteine of Darfler in the method of Smith et al.

The skilled artisan would have been motivated to make such a modification because the antioxidant such as N-acetyl-L-cysteine improves lymphoid survival and growth when culture in serum-free medium, as a protective agent and very effective at removing the toxicity due to oxidizing agents present in basal tissue culture media (see column 5, lines 58-67).

The person of ordinary skill in the art would have had a reasonable expectation of success in adding N-acetyl-L-cysteine in the medium of Smith et al. to improve the survival and growth of hematopoietic cells.

Furthermore, it would have been obvious to a person of ordinary skill in the art to try N-acetyl-cysteine of Darfler as an antioxidant in the medium of Smith et al. because a person of ordinary skill in the art recognizes that there are finite number of identified or known antioxidants available for cell culture medium and N-acetyl-cysteine of Darfler being one of such antioxidants.

The Supreme Court recently states in KSR v. Teleflex (550 US82 USPQ2d 1385, 2007) "The same constricted analysis led the Court of Appeals to conclude, in error, that a patent claim cannot be proved obvious merely by showing that the combination of elements was "obvious to try." Id., at 289 (internal quotation marks omitted). When there

is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under §103."

Although Smith et al. in view of Darfler do not particularly teach all the ingredients listed in claim 55, it would have been obvious for a person of ordinary skill in the art to modify the serum-free medium of Smith et al. in view of Darfler to optimize the outcome of hematopoietic cell culture by addition various well known components used in cell culture. Since the ingredients listed in claim 55 are individually well known in the art to be used as common components of cell culture media, a person of ordinary skill in the art would have had motivation to modify by adding or removing one or more ingredients in the serum-free medium of Smith et al. in view of Darfler. Unless there is clear evidence that the medium of Smith et al. in view of Darfler is different from the medium of the current invention, the examiner takes the position that the medium of Smith et al. in view of Darfler is the same as the claimed invention.

Although Smith et al. in view of Darfler do not particularly teach the use of recombinant CD34+ hematopoietic cells, it would have been obvious for a person of ordinary skill in the art use any kind of hematopoietic cells expressing CD34 surface marker because the fact that whether the cells are recombinant or not would not provide any patentable weight on the claimed method of expanding hematopoietic cells.

Furthermore, the recombination technique is well known in the art even for hematopoietic cells as supported by Walsh et al. or Hamilton et al. teaching virally transduced hematopoietic progenitor cells, and since the method of Smith et al. is capable of expanding hematopoietic cells, it is clear that the method of Smith et al. would be able to carry out the intended use of expanding the recombinant CD34+ hematopoietic cells of the current invention.

M.P.E.P. § 2111.02 reads, "If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the claimed invention's limitations, then the preamble is not considered a limitation and is of no significance to claim construction." As such, the limitation "the recombinant CD34+ hematopoietic cells" does not affect the patentability of the claimed composition/method. Compositions are defined by their physical, structural, and chemical properties, not by an intended use or application. Methods are defined by their constituent steps, not by an intended use or application.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TAEYOON KIM whose telephone number is (571)272-9041. The examiner can normally be reached on 8:00 am - 4:00 pm ET (Mon-Thu).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford Jr/
Primary Examiner, Art Unit 1651

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